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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,662	04/27/2001	Eva Raschke	8325-0012	9004

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EXAMINER	
WAX, ROBERT A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,662	RASCHKE ET AL.	
	Examiner	Art Unit	
	Robert A. Wax	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-18,20-24,27 and 57-86* is/are pending in the application.

4a) Of the above claim(s) *1-3,6-18,20-24,27,58,59,61 and 72-86* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57,60 and 62-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3 of them*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 6 in the reply filed on May 10, 2004 is acknowledged. The traversal is on the ground(s) that (1) the requirement is unclear, (2) the Office appears to have placed undue emphasis on the relatively small number of claimed species of exogenous molecules, (3) that the Office is somehow preventing applicants from claiming what they believe to be their invention, (4) that the Office has not established that the protein delivery claims of Group 1a are distinct from the nucleic acid delivery claims of Group 1b and (5) that the Office has not met its burden of showing that the claimed product can be made by another materially different process. These arguments are not found persuasive to alter the restriction for the reasons explained below.

First, Examiner agrees that the restriction requirement was unclear. Claim 8 was omitted and should have been included with Group 1 (and also in Groups 1a and 1b, see below). Also, claim 18 was incorrectly identified as a linking claim for inventions 1-3, and should have been included in Group 1 instead. Finally, it was stated that if applicants elected Group 1, a further election was required between methods in which the protein was introduced into a cell by means of an expression vector (as in claim 11) or simply as a protein. These were labeled as inventions '1a' and '1b', and linking claims 12-17 were incorrectly included in each group. By way of clarification, Group 1 includes claims 6-11, 18, 20-24, 27, 79-81 and 83, Group 1a includes claims 6-10, 18, 21-24, 27

and 79-81 and Group 1b includes claims 11, 20 and 83. Claims 12-17 are linking claims and should not have been listed in either of these groups and have, therefore, been removed.

Examiner does not agree with the subsequent arguments. The number of claimed species of exogenous molecules has nothing to do with the basis of the restriction. Restriction is permitted if the independent inventions have different modes or operation and are not disclosed as capable of use together. Clearly, the protein, nucleic acid and small molecule do not behave the same way as each other when introduced into a cell since they are chemically very different. Each may be targeted to a particular location by its hydrophobicity, for example, which will be different for each type of molecule.

Applicants' third argument, that the Office is somehow preventing applicants from claiming what they believe to be their invention, is not correct. Applicants are not prevented from claiming whatever they want; a restriction requirement does not change what may be claimed. The restriction requirement only addresses which of the claims will be examined together. The three types of molecules are intended to bind chromatin but they do not share any structural features with each other. The chromatin to be bound is common to all three but each type of binding molecule is chemically very different from the others. Applicants' assertion that the search burden will not be reduced by the restriction is simply incorrect. Only the elected portion of the subject matter of the linking claim is searched but the linking claim itself is not searched in its entirety. The instant election of the protein dictates that the search will focus on protein

bound to chromatin, not DNA bound to chromatin, nor to a small molecule bound to chromatin.

Applicants next argue that the Office has not established that the protein delivery claims of Group 1a are distinct from the nucleic acid delivery claims of Group 1b. Applicants have requested the Office provide evidence that the binding interaction of a peptide encoded by a nucleic acid introduced into a cell would be materially different than the binding interaction of the same peptide, introduced into a cell in peptide form. Applicants have misinterpreted the difference. Examiner agrees that there would be no difference in the binding of a protein to chromatin whether the protein were introduced as such or expressed from nucleic acid encoding the same protein. The difference is that the nucleic acid introduced into the cell might not express the protein. This is particularly evident in the case of gene therapy, which relies on the expression of foreign DNA in cells and is notoriously unsuccessful. Nevertheless, each mode of provision of the protein has its own issues. Administration of protein itself is much more predictable than administration of nucleic acid encoding the protein. It is these differences that support the restriction between them.

Applicants' final argument is that the Office has not met its burden of showing that the claimed product can be made by another materially different process. The argument is that if the chromatin is removed from the cell then it's no longer cellular chromatin and if the binding molecule were naturally occurring then it would not be exogenous. Examiner does not agree with this argument either. The method claims recite steps other than actually introducing the molecule into the cell, namely,

identification of an accessible region and a target site. An example of a materially different process would be to introduce a library of several appropriately labeled molecules and seeing which ones bound, thus eliminating the first two steps of the claimed process. Thus, the Office has indeed met its burden.

The requirement is still deemed proper and is therefore made FINAL.

As requested by Applicants, Examiner hereby confirms that, if any of linking claims 57, 60, 65, 66 or 69-71 are allowed, the Restriction Requirement between Groups 4-6 will be withdrawn (MPEP 809) and all claims in Groups 4, 5 and 6, including any and all allowed linking claims, will be examined. Examiner hereby also confirms that, should an elected product claim be found allowable, process claims of the same scope will be rejoined, in accordance with the Office's practice regarding *In re Ochiai*. The following information should have been presented in the written restriction, and its inclusion now is deemed still timely since nothing has been found allowable.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Information Disclosure Statement

2. The information disclosure statements filed May 10, 2002, July 1, 2002 and August 8, 2002 have been considered. Please see the attached initialed PTO-1449s.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The hyperlink is at page 15, line 13.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

5. Claims 57, 62-68, 70 and 71 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Aoki et al.

Aoki et al. disclose a complex of RP58 (Repressor Protein with molecular mass of 58 – see abstract), a DNA binding protein having zinc finger motifs (page 26701, left column, lines 1-5) in a human cell. This clearly anticipates the above claims. Claim 68 is included because the source of the protein in the complex does not further limit the composition and, therefore, has no patentable weight.

6. Claims 57, 62, 63, 66-68, 70 and 71 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Robertson et al.

Robertson et al. teach that the DNA of Kaposi's sarcoma-associated herpes virus (KSHV) persists through several generations of host cell by tethering the DNA to the host chromosome (or chromatin) with a viral protein called LANA, see column 2, lines 42-55 and column 8, lines 41-52. This anticipates the above claims because the LANA protein is exogenous, encoded by DNA introduced into the cell (virally) and the protein/chromatin forms a complex. Claim 63 is included because LANA is presumably a transcription factor, see column 8, lines 31-38.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 69 is rejected under 35 U.S.C. 103(a) as being unpatentable over Robertson et al.

The teachings of Robertson et al. have been outlined above. At column 10, lines 55-58 they state that the multicellular organism may be a plant. Elsewhere in their specification they state that their concepts are not limited to the exact disclosure.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to select a plant virus that makes LANA such as tobacco mosaic virus, and do the same experiment done by Robertson et al., except in plant cells, with the reasonable expectation of making a protein/chromatin complex and regulating transcription of the encoded protein.

10. Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki et al. in view of Greisman et al. and Neely et al.

The teachings of Aoki et al. have been outlined above.

Greisman et al. teach a strategy for selecting high-affinity zinc finger proteins for diverse DNA target sites.

Neely et al. teach that zinc finger 4 of Transcription Factor IIIA binds in the minor groove.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to select the protein of Neely et al. using the method of Greisman et al. and expect to achieve the protein/chromatin complex of Aoki et al.

11. Claim 65 is rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki et al. in view of Greisman et al. and Gross et al.

The teachings of Aoki et al. and Greisman et al. have been outlined above.

Gross et al. teach of nuclease hypersensitive sites in chromatin and their uses.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to select a nuclease hypersensitive site according to the teachings of Gross et al., for the reasons noted therein, and select a zinc finger protein that binds thereto, according to the teachings of Greisman et al. in order to create a protein/chromatin complex as taught by Aoki et al. with the expectation of achieving protection against nuclease cleavage of the DNA.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Wax whose telephone number is (571) 272-0623. The examiner can normally be reached on Monday through Friday, between 9:00 AM and 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Wax
Primary Examiner
Art Unit 1653

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